IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	MEYER et al.
Serial No.	:	10/569,714 (U.S. Patent Application Publication 2007-0077284)
Filing Date	:	September 21, 2006
For	:	**TRANSDERMAL FORMULATION COMPRISING AN OPIOID ANALGESIC AND AN ALOE COMPOSITION**
Examiner	:	CHEN, Catheryne
Art Unit	:	1655

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DECLARATION UNDER 37 C.F.R. § 1.132

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I, Dr. Elisabeth Meyer of Kreuzberg 31c, D-83714 Miesbach, a citizen of Germany, hereby declare:

- that I am a biologist having studied at the University of Ulm (Diploma 1992);
- that I received the degree of Doctor of Natural Scienees (Dr. rer nat) in Biology at the University of Ulm in 1995;
- that I entered the employ of Acino AG, Miesbach, DE in 2002, where I am still employed and currently hold the position of Patent Affairs Manager;
- that I am currently listed as an inventor on approx. 10 U.S. patent application publications according to the USPTO database;
- that I am listed as an author on 10 peer reviewed publications;
- that I have specialized for more than 6 years in the field of skin care formulations and active ingredients.

I am an inventor in this application and have reviewed the application and final rejection of 27 October 2008.

When considering the applicants invention as a whole, the present invention provides a solution for the problem of imparting a pharmaceutical formulation with properties which enable an opiod analgesic to be transdermally administered. The solution for this problem consists in

- a transdermal formulation comprising
- a synthetic rubber adhesive selected from a styrene-butadiene-styrene block copolymer or a styrene-butadiene block copolymer,
- an opioid analgesic from the phenanthrene group or a pharmaceutically acceptable salt thereof as active ingredient and
- an aloe composition as transdermal penetration agent.

With respect to amended claim 1, the formulation comprises a synthetic rubber adhesive selected from a styrene-butadiene-styrene block copolymer or a styrene-butadiene block copolymer.

I have carried out comparative experiments which are similar to Example 1 in the specification and which are now presented for the first time with this submission this Declaration.

In Example 1 of the description of the present application experiments with different matrix patches are presented. The results are summarized in Table I on page 16 of the description. A matrix patch is provided which comprises a mixture of buprenorphine (the analgesic), an aloe (the transdermal penetration agent) and a styrene-butadiene-styrene polymer (the adhesive). Flux experiments with hairless mouse skin reveal buprenorphine fluxes in the range from 0.8 to 2.3 $\mu g/cm^2*h$ and the transdermal penetration effect of aloe compositions.

In the comparative experiments the styrene-butadiene-styrene polymer (the adhesive) was replaced by several acrylate adhesives, i.e. the adhesive which is disclosed by Fischer as the usual adhesive in combination with the intradermal penetration agent (the aloe composition) and the drug.

The results as disclosed in the description and the results of the comparative experiments are presented in the following table below (see next page):

Adhesive type	PSA	Buprenorphine (% w/w)	*Aloe vera* (% w/w)	Flux (hairless mouse skin)	Formation of crystals
Examples of the Present Invention (cf. Table I of the invention, page 16)					
Styrene-butadiene-styrene polymer	DT 6173	15	20	2.3 µg/(cm^2*h)	–
Styrene-butadiene-styrene polymer	DT 6173	5	20	0.8 µg/(cm^2*h)	–
Styrene-butadiene-styrene polymer	DT 6173	10	10	0.9 µg/(cm^2*h)	–
Comparative Examples					
Acrylate-vinylacetate with carboxy groups	DT 2825	10	10	1.1 µg/(cm^2*h)	+
Acrylate-vinylacetate with hydroxyl groups	DT 2287	10	10	1.1 µg/(cm^2*h)	+
Acrylate with functional hydroxy groups	DT 2510	10	10	1.3 µg/(cm^2*h)	+
Acrylate-vinylacetate without functional groups	DT 4098	10	10	1.5 µg/(cm^2*h)	+

It should first be noted that in the description of the present application the fluxes are accidentally given as g/(cm^2*h). In fact, also in the case of the invention the fluxes are in the micro gram range and should read as µg/(cm^2*h) which is corrected in the specification.

When comparing the results of the above experiments in which the patches comprise 10 % (w/w) *Aloe vera* it turns out that the fluxes which are obtained with the styrene-butadiene-styrene polymers as adhesive (according to the invention) and with the acrylates as adhesives (comparative examples) are similar. However, with the acrylate polymers a disadvantageous crystallisation of the drug (buprenorphine) in the matrix is observed over the time. Such a crystallisation reduces the long term stability of the formulations and the amount of drug available for the transdermal penetration and is very disadvantageous for transdermal applications, for which a relatively high concentration of the dissolved drug in the pharmaceutical formulation is needed. This disadvantageous crystallisation effect can be avoided using the styrene-butadiene-styrene polymers of the invention.

The Fischer invention does not comprise any hint that, different from acrylates, styrene-butadiene-styrene polymer adhesives in pharmaceutical formulations can prevent crystallisation of the drug, whereby the long term stability of formulations comprising buprenorphine and an aloe composition are improved and whereby the formulations may be used as transdermal formulations.

The undersigned hereby declares as follows:

The undersigned further declares that all statements made herein of his or her own knowledge are true and that all statements made on information and belief are believed to be true; and that the foregoing statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 26 August 2009 By: E. Meyer

Dr. Elisabeth Meyer